UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,444	01/22/2002	Paul M. Guyre	DC-0172	9998

7590 01/14/2003

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	6

DATE MAILED: 01/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/054,444	Applicant(s) GUYRE ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/24/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-5* is/are pending in the application.

4a) Of the above claim(s) *4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1 and 3-5 are pending.

2. Claims 4-5 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions. Applicant is reminded that a formal request must be made in order to cancel non-elected claims 4-5.

3. In view of the amendment filed 10/24/02, the following rejections remains.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of "recombinant Fel dI wherein the baculovirus expressed recombinant Fel dI comprises chain 1 an chain 2" because recombinant Fel dI comprises chain 1 and chain 2 without SEQ ID NO have no structure much less function.

The specification discloses only a composition comprising a baculovirus expression vector expressed a specific recombinant Fel dI comprising chain-1 Fel dI chain 1 and chain-2 linked together in series via a flexible peptide linker $(glycine_4\ Ser)_3$ and further linked to sFv H22 (H22-FelDI ch1+Ch2 sequences) for diagnosis of cat allergy in humans. The recombinant Fel dI is purified on nickel affinity column. The rFel dI shows that IgG and IgE antibody binding is identical to natural Fel dI using IgG antibody in pooled sera from either Japanese or US cat allergic patients.

With the exception of the specific composition mentioned above for diagnosing cat allergy, there is insufficient written description about the structure associated with functions of *any* "recombinant Fel dI" for a composition for diagnosing cat allergy. Further, the specification

discloses only one compound as shown in Fig 1. Given the lack of a written description of *any* additional representative species of recombinant Fel dI encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 10/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 2 has been canceled. (2) Claims 1 and 3 have been amended.

However, the amended claim 1 still recites ...a recombinant Fel dI comprises chain 1 and chain 2 ...without a SEQ ID NO.

6. The following new grounds of objection and rejection are necessitated by the amendment filed 10/24/02.

7. Claim 1 is objected to because SEQ ID NO: 5 is an oligonucleotide of glycine/serine linker whereas the compound as recited in claim 1 is a **polypeptide** such as recombinant Fel dI comprises chain 1 and chain 2 linked together by a glycine/serine linker.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,547,669 (of record, Aug 1996, PTO 892) in view of US Pat No 5,395,750 (Mar 1995; PTO 892).

The '669 patent teaches various compounds such as TRFP also known as Fel dI chain 1 (reference SEQ ID NO: 2), Fel dI chain 2 (reference SEQ ID NO: 6) and fusion protein such as recombinant cat allergen Fel dI fusion protein comprising chains 1 and 2 linked together via a linker such as any non-epitope amino acid sequence or other appropriate linking or joining agent (See column 10, lines 13-66, in particular). The '669 patent teaches the recombinant Fel dI is useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular).

The claimed invention as recited in claim 1 differs from the reference only that the linker is a glycine/serine linker of SEQ ID NO: 5.

The '750 patent teaches a method of making a compound such as synthetic single chain antibody sequence such as heavy and light region sequences of any antibody is linked by a glycine (G) /serine (S) linker sequence such as GGGGSGGGGSGGGGS that is identical to the claimed linker sequence of SEQ ID NO: 5 (See reference SEQ ID NO: 13, column 8, lines 65-68, in particular) wherein the reference compound is expressed in E coli, in S cerevisiae and phage display library (See column 9, lines 1-4, lines 50-55, in particular). The '750 patent teaches the reference linker sequence is flexible (See column 8, lines 65-66, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to link chain 1 and chain 2 in series as taught by the '669 patent using a linker such as glycine and serine $(glycine_4\,Ser)_3$ as taught by the '750 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '669 patent teaches the recombinant Fel dI is useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular). The '750 patent teaches the linker sequence such as GGGGSGGGGSGGGGS is flexible (See column 9, lines 1-4, lines 50-55, in particular). The recitation of a compound being expressed by

baculovirus has no patentable weight because a compound is a compound, irrespective of how it is made.

Applicants' arguments filed 10/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 2 has been canceled. (2) The '669 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5, (3) the '243 patent teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5. Although Figure 40A does show use of a linker that includes (Gly4Ser)3, nowhere, including Figures 39A, 39B, 40A, 40B and 40C, does this patent show use of a linker comprising SEQ ID NO: 5. Figure 40A shows a linker present but does not define where it stops. (4) There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

However, the '669 patent teaches various compounds such as TRFP also known as Fel dI chain 1 (reference SEQ ID NO: 2), Fel dI chain 2 (reference SEQ ID NO: 6) and fusion protein such as recombinant cat allergen Fel dI fusion protein comprising chains 1 and 2 linked together via a linker such as any non-epitope amino acid sequence or other appropriate linking or joining agent (See column 10, lines 13-66, in particular). The '750 patent teaches a method of making a compound such as synthetic single chain antibody sequence such as heavy and light region sequences of any antibody is linked by a flexible glycine (G) /serine (S) linker sequence such as GGGGSGGGGSGGGGS that is identical to the claimed linker sequence of SEQ ID NO: 5 (See reference SEQ ID NO: 13, column 8, lines 65-68, in particular) wherein the reference compound is expressed in E coli, in S cerevisiae and phage display library (See column 9, lines 1-4, lines 50-55, in particular).

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,547,669 (of record, Aug 1996, PTO 892) in view of in view of US Pat No 5,395,750 (Mar 1995; PTO 892) as applied to claim 1 above and further in view of US Pat No. 5,837,243 (of record, Nov 1998; PTO 892).

The teachings of the '669 patent and the '750 patent have been discussed supra.

The claimed invention as recited in claim 3 differs from the references only that the compound further comprising a sFv of monoclonal antibody H22 which is a humanized anti-CD64 antibody.

The '243 patent teaches bispecific molecules such as cat allergen linked to humanized or single chain (sFv) antibody H22 that binds to Fc receptor such as FcγRI (which also known as CD64) (See column 7, lines 52-67 bridging column 8, lines 1-19, claim 3 of '243, column 6, lines 64-67, in particular). The '243 patent further teaches a method of making bispecific molecules using various expression constructs such as pSVgpt and pSVhyg encoding single chain antibody (sFv) H22 that is specific for humanized Fc receptor such as FcγRI (See column 18, lines 24-33, in particular). The '243 patent teaches the fusion molecules is linked together via a linker such as glycine and serine $(glycine_4\,Ser)_3$ (See Fig 40A, in particular). The '243 patent teaches the antibody H22 is useful for targeting any antigen to the antigen presenting cell by binding to a surface receptor such as FcγRI on the antigen presenting cells, in turn, the antigen presenting cells can internalize antigen for processing and presentation to induce tolerance to said antigen (See column 7, lines 57-67 bridging column 8, lines 1-2, column 8, lines 57-62, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to link the single chain humanized antibody H22 that is specific for Fc receptor such as FcγRI (CD64) to chain 1 and chain 2 of Fel dI (cat allergen) in series as taught by the '669 using a flexible glycine and serine linker $(glycine_4\,Ser)_3$ as taught by the '750 patent for a compound comprising a recombinant Fel dI comprises chain 1 and chain 2 expressed in series and linked together by a glycine/serine linker and further comprising a sFv of monoclonal antibody H22 which is a humanized anti-CD64 antibody. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '243 patent teaches the antibody H22 is useful for targeting any antigen to the antigen presenting cell by binding to a surface receptor such as FcγRI on the antigen presenting cells, in turn, the antigen presenting cells can internalize antigen for processing and presentation to induce

tolerance to any antigen such as allergen (See column 7, lines 57-67 bridging column 8, lines 1-2, column 8, lines 57-62, in particular).

Applicants' arguments filed 10/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 2 has been canceled. (2) The '669 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5, (3) The '243 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5. Although Figure 40A does show use of a linker that includes (Gly4Ser)3, nowhere, including Figures 39A, 39B, 40A, 40B and 40C, does this patent show use of a linker comprising SEQ ID NO: 5. Figure 40A shows a linker present but does not define where it stops. (4) There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

In response to Applicants' argument that the '669 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5, the '669 patent teaches various compounds such as TRFP also known as Fel dI chain 1 (reference SEQ ID NO: 2), Fel dI chain 2 (reference SEQ ID NO: 6) and fusion protein such as recombinant cat allergen Fel dI fusion protein comprising chains 1 and 2 linked together via a linker such as any non-epitope amino acid sequence or other appropriate linking or joining agent (See column 10, lines 13-66, in particular). The '243 patent teaches the fusion molecules is linked together via a linker such as glycine and serine $(glycine_4 Ser)_3$ (See Fig 40A, in particular). The '750 patent teaches a method of making a compound such as synthetic single chain antibody sequence such as heavy and light region sequences of any antibody is linked by a flexible glycine (G) /serine (S) linker sequence such as GGGGSGGGGSGGGGS that is identical to the claimed linker sequence of SEQ ID NO: 5 (See reference SEQ ID NO: 13, column 8, lines 65-68, in particular) wherein the reference compound is expressed in E coli, in S cerevisiae and phage display library (See column 9, lines 1-4, lines 50-55, in particular).

In response to applicants' argument that there is no suggestion or motivation, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching,

suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the teachings of the '243 patent pertaining to linking the cat allergen to single chain antibody sFv H22 that binds to CD64 (See column 7, lines 52-67 bridging column 8, lines 1-19, claim 3 of '243, column 6, lines 64-67, in particular) are useful for targeting allergen to the antigen presenting cell by binding to a surface receptor such as FcγRI on the antigen presenting cells, in turn, the antigen presenting cells can internalize antigen for processing and presentation to induce tolerance to said antigen (See column 7, lines 57-67 bridging column 8, lines 1-2, column 8, lines 57-62, in particular). The teachings of the '699 patent pertaining to recombinant Fel dI comprising chain 1 and chain 2 linked together by any linker that is expressed as a recombinant protein are useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular). The teachings of the '760 pertaining to the linker such as glycine/serine are useful for linking any polypeptide because it is flexible (See reference SEQ ID NO: 13, column 8, lines 65-68, in particular). The teachings of the Bei *et al* pertaining *to* the baculovirus expression system for making any protein included high efficiency of expression, ease of purification, time saving and cost-effective method of scaling up production of functional proteins (See page 253, column 2, last paragraph, in particular). In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983), the strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination.

12. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,547,669 (of record, Aug 1996, PTO 892) in view of US Pat No 5,395,750 (Mar 1995; PTO 892) and Bei *et al* (of record, J Immunological Methods 186: 245-255, Oct 1995; PTO 892).

The teachings of the '669 patent and the '750 patents have been discussed supra. The '669 patent further teaches the recombinant Fel dI is expressed in *E. Coli* (See column 2, lines 15-25, lines 65-67 bridging column 22, lines 1-7, column 12, lines 40-43, column 18, line 23, in particular). The '669 patent teaches the recombinant Fel dI is useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular).

The claimed invention as recited in claim 1 differs from the reference only that the compound is expressed by a baculovirus.

Bei *et al* teach the salient features of the baculovirus expression system for making any protein included high efficiency of expression, ease of purification, time saving and cost-effective method of scaling up production of functional proteins (See page 253, column 2, last paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the *E. Coli* expression vector as taught by the '669 patent or the S cerevisiae vector or phage display vector as taught by the '750 patent for a compound comprising the recombinant Fel dI comprises chain 1 and chain 2 expressed in series and linked together by a glycine/serine linker of SEQ ID NO: 5 as taught by the '669 patent, the 750 patent and Bei *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Bei *et al* teach the salient features of the baculovirus expression system included high efficiency of expression, ease of purification, time saving and cost-effective method of scaling up production of functional proteins (See page 253, column 2, last paragraph, in particular). The '669 patent teaches the recombinant Fel dI is useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular).

Applicants' arguments filed 10/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 2 has been canceled. (2) The '669 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5, (3) The '243 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5. Although Figure 40A does show use of a linker that includes (Gly4Ser)3, nowhere, including Figures 39A, 39B, 40A, 40B and 40C, does this patent show use of a linker comprising SEQ ID NO: 5. Figure 40A shows a linker present but does not define where it stops. (4) There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

In response to Applicants' argument that the '669 patent does not teach or suggest the specific recombinant compound as claimed which is a baculovirus expressed in series and linked by a glycine/serine linker of SEQ ID NO: 5, the '669 patent teaches various compounds such as TRFP also known as Fel dI chain 1 (reference SEQ ID NO: 2), Fel dI chain 2 (reference SEQ ID NO: 6) and fusion protein such as recombinant cat allergen Fel dI fusion protein comprising chains 1 and 2 linked together via a linker such as any non-epitope amino acid sequence or other appropriate linking or joining agent (See column 10, lines 13-66, in particular). The '243 patent teaches the fusion molecules is linked together via a linker such as glycine and serine $(glycine_4 Ser)_3$ (See Fig 40A, in particular). The '750 patent teaches a method of making a compound such as synthetic single chain antibody sequence such as heavy and light region sequences of any antibody is linked by a flexible glycine (G) /serine (S) linker sequence such as GGGGSGGGGSGGGGS that is identical to the claimed linker sequence of SEQ ID NO: 5 (See reference SEQ ID NO: 13, column 8, lines 65-68, in particular) wherein the reference compound is expressed in E coli, in S cerevisiae and phage display library (See column 9, lines 1-4, lines 50-55, in particular).

In response to applicants' argument that there is no suggestion or motivation, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the teachings of the '243 patent pertaining to linking the cat allergen to single chain antibody sFv H22 that binds to CD64 (See column 7, lines 52-67 bridging column 8, lines 1-19, claim 3 of '243, column 6, lines 64-67, in particular) are useful for targeting allergen to the antigen presenting cell by binding to a surface receptor such as FcγRI on the antigen presenting cells, in turn, the antigen presenting cells can internalize antigen for processing and presentation to induce tolerance to said antigen (See column 7, lines 57-67 bridging column 8, lines 1-2, column 8, lines 57-62, in particular). The teachings of the '699 patent pertaining to recombinant Fel dI comprising chain 1 and chain 2 linked together by any linker that is expressed as a recombinant protein are useful for treating and diagnosing sensitivity in an individual to cat allergen such as Fel dI (See column 12, lines 31-33, in particular). The teachings of the '760 pertaining to the linker such as glycine/serine are useful for linking any polypeptide because it is flexible (See reference SEQ ID NO: 13, column 8, lines

65-68, in particular). The teachings of the Bei *et al* pertaining *to* the baculovirus expression system for making any protein included high efficiency of expression, ease of purification, time saving and cost-effective method of scaling up production of functional proteins (See page 253, column 2, last paragraph, in particular). In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983), the strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

16. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
January 13, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600